4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2022-N-0799]

Improving 510(k) Submission Preparation and Review: Center for Biologics Evaluation and Research; Voluntary Electronic Submission Template and Resource Pilot Program; Request for Comments

AGENCY: Food and Drug Administration, Department of Health and Human Services (HHS).

ACTION: Notice; request for comments.

SUMMARY: The Food and Drug Administration's (FDA or Agency) Center for Biologics Evaluation and Research (CBER) is announcing a pilot program for sponsors of CBER premarket notification (510(k)) submissions that wish to use the voluntary Electronic Submission Template and Resource (eSTAR) Pilot Program. CBER's voluntary eSTAR Pilot Program is intended to improve consistency and efficiency in both industry's preparation and FDA's review of premarket notification (510(k)) submissions. During CBER's voluntary eSTAR Pilot Program, participants will have the opportunity to provide input to FDA on the eSTAR Pilot Program for submissions to CBER.

DATES: FDA is seeking participation in CBER's voluntary eSTAR Pilot Program beginning [INSERT DATE OF PUBLICATION IN THE *FEDERAL REGISTER*]. See section I.A. for instructions on how to submit a request to participate. The CBER voluntary eSTAR Pilot Program will select up to nine participants who best match the selection criteria. This pilot program will begin [INSERT DATE OF PUBLICATION IN THE *FEDERAL REGISTER*]. Submit either electronic or written comments on the notice by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*].

ADDRESSES: You may submit comments as follows. Please note that late, untimely filed comments will not be considered. The https://www.regulations.gov electronic filing system will

accept comments until 11:59 p.m. Eastern Time at the end of [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*]. Comments received by mail/hand delivery/courier (for written/paper submissions) will be considered timely if they are postmarked or the delivery service acceptance receipt is on or before that date.

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: https://www.regulations.gov. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to https://www.regulations.gov will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on https://www.regulations.gov.
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

Written/Paper Submissions

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in "Instructions."

Instructions: All submissions received must include the Docket No. FDA-2022-N-0799 for "Improving 510(k) Submission Preparation and Review: Center for Biologics Evaluation and Research; Voluntary Electronic Submission Template and Resource Pilot Program." Received comments, those filed in a timely manner (see ADDRESSES), will be placed in the docket and, except for those submitted as "Confidential Submissions," publicly viewable at https://www.regulations.gov or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday, 240-402-7500.

- Confidential Submissions--To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states "THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION." The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on https://www.regulations.gov. Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as "confidential." Any information marked as "confidential" will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: https://www.govinfo.gov/content/pkg/FR-2015-09-18/pdf/2015-23389.pdf.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to https://www.regulations.gov and insert the docket number, found in brackets in the heading of this document, into the "Search" box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852, 240-402-7500.

FOR FURTHER INFORMATION CONTACT: Myrna Hanna, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 7301, Silver Spring, MD 20993-0002, 240-402-7911.

SUPPLEMENTARY INFORMATION:

I. Background

In the Medical Device User Fee Amendments of 2012 (MDUFA III) Commitment Letter from the Secretary of Health and Human Services to Congress, FDA committed to streamlining review processes by moving beyond paper-based review (Ref. 1). Under section 745A(b) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 379k-1), added by section 1136 of the Food and Drug Administration Safety and Innovation Act (Pub. L. 112-144), an electronic copy (eCopy) is required for certain premarket submission types, including 510(k) submissions. FDA provided additional information about the submissions subject to the eCopy requirements in section 745A(b) of the FD&C Act and recommendations about the use of eCopy generally in a guidance initially issued in 2013 (Ref. 2). FDA subsequently published a final rule in the *Federal Register* of December 16, 2019 (84 FR 68334), amending FDA's regulations, where appropriate, to reflect the requirement of a single submission in electronic format, including the use of eCopy requirements.

In the Medical Device User Fee Amendments of 2017 (MDUFA IV) Commitment Letter from the Secretary of Health and Human Services to Congress (Ref. 3), FDA committed to developing "electronic submission templates that will serve as guided submission preparation tools for industry to improve submission consistency and enhance efficiency in the review

process." In addition, section 745A(b) of the FD&C Act, as amended by section 207 of the FDA Reauthorization Act of 2017 (Pub. L. 115-52), requires that certain presubmissions and submissions for devices, including 510(k) submissions, be submitted in such electronic format as specified in guidance by FDA.

FDA considers both eCopies and eSubmissions to be submissions in electronic format. eSubmissions are submission packages produced by an electronic submission template that contains the data of a "complete" (see Ref. 4) submission. To support the next step in transition to 510(k) submissions solely in electronic format, FDA has developed eSTAR, an electronic submission template built within a structured dynamic PDF that guides a user through construction of an eSubmission. eSTAR includes the following benefits:

- automation (e.g., form construction, autofilling);
- content and structure that is complementary to FDA internal review templates;
- integration of multiple resources (e.g., guidances, databases);
- guided construction for each submission section;
- automatic verification (i.e., FDA does not intend to conduct a Refuse to Accept (RTA) review (Ref. 4)); and
- it is free to use.

eSTAR contains the following additional benefits:

- intuitive interface;
- no special software installation (if the user has Adobe Acrobat or similar software already installed);
- support for images and dynamic pop-up messages;
- mobile device and Apple iOS support;
- ability to comment when converted to a static PDF;
- ability to share (e.g., email) an eSTAR file that is in the process of being constructed; and

- no packaging process.

In February 2020, CDRH piloted the use of the eSTAR electronic submission template (85 FR 11371). FDA then issued a draft guidance in September 2021 describing the technical standards associated with preparation of the electronic submission template for 510(k)s (Ref. 5) that, when the guidance is finalized, will enable submission of 510(k) electronic submissions solely in electronic format. In the draft guidance, FDA noted that CBER also intended to pilot eSTAR. FDA is now announcing CBER's voluntary eSTAR Pilot Program and soliciting participation from 510(k) submitters for this program. This pilot will provide an opportunity for CBER staff to gain experience with review of and internal processes for 510(k) submissions using the eSTAR template. It will also provide experience with use of the FDA Electronic Submissions Gateway for 510(k) submissions using the eSTAR template. Information collected through the pilot program will help inform FDA on how to improve eSTAR and identify any additional considerations specific to submissions for CBER-regulated devices.

A. CBER Voluntary eSTAR Pilot Program Participation

FDA seeks participation from 510(k) submitters in CBER's voluntary eSTAR Pilot Program beginning [INSERT DATE OF PUBLICATION IN THE *FEDERAL REGISTER*]. The CBER voluntary eSTAR Pilot Program will select up to nine participants whose submissions to CBER meet the selection criteria.

Companies that may be eligible to participate in CBER's voluntary eSTAR Pilot Program are limited to those firms following the procedures set out in section I.B. of this document and that also meet all the selection criteria that follow:

1. intent to submit a traditional, special, or abbreviated 510(k) for a medical device regulated by CBER (Ref. 6) using eSTAR within 1 month of acceptance to the CBER voluntary eSTAR Pilot Program; and
2. willingness to provide feedback on eSTAR as outlined in section I.C. of this document.

At its discretion, FDA may withdraw a manufacturer from the CBER voluntary eSTAR Pilot Program for not carrying out any of the commitments mentioned previously.

B. CBER Voluntary eSTAR Pilot Program Procedure

To be considered for CBER's voluntary eSTAR Pilot Program, a company should submit a statement of interest for participation to Industry.biologics@fda.hhs.gov. The statement of interest should include "CBER Voluntary eSTAR Pilot Program" in the subject line and agreement to the selection criteria listed in section I.A. of this document, as well as a description of the device in enough detail to allow verification that it is a CBER regulated device.

The following captures the process for the CBER voluntary eSTAR Pilot Program:

1. FDA will collect statements of interest for participation in the pilot program beginning [INSERT DATE OF PUBLICATION IN THE *FEDERAL REGISTER*].

   The statement of interest should include:

   - agreement to the selection criteria listed in section I.A. of this document
   - the device(s) that is/are likely to be submitted during the pilot program using eSTAR

2. FDA will select no more than nine participants, who best meet the selection criteria and who reflect the broad spectrum of device manufacturers, including companies that develop a range of products. Enrollment in the pilot program will be ongoing throughout the duration of the program. FDA will apply lessons learned from the initial participants in the pilot program to refine eSTAR with participants, as appropriate.
3. FDA intends to notify the manufacturer via email if the manufacturer is enrolled as a participant in the CBER's voluntary eSTAR Pilot Program.
4. The enrolled manufacturer should navigate to the FDA "Voluntary eSTAR Program" web page at:

   https://www.fda.gov/medical-devices/how-study-and-market-your-device/premarket-submissions and download eSTAR from the "Voluntary eSTAR Program" web page

(Ref. 7). *Note:* eSTAR should not be submitted to CBER unless the sponsor is a pilot participant.

5. Directions for preparing and submitting a 510(k) using eSTAR to FDA are in the final section of the eSTAR pdf. We recommend that all eSTAR elements including the cover letter be submitted through the FDA Electronic Submissions Gateway (refer to "Electronic Submissions Gateway") (Ref. 8) or on physical media through CBER's Document Control Center in accordance with the "Regulatory Submissions in Electronic and Paper Format for CBER-Regulated Products" web page (Ref. 9). We recommend that you use Adobe Acrobat Pro with eSTAR. Be aware that eSTARs should not be submitted to CDRH via the Electronic Submission Gateway, as CDRH does not use the Electronic Submission Gateway to receive submissions.
6. If eligible and enrolled as a participant, the manufacturer should submit a 510(k) submission prepared and verified using eSTAR within the timeframe identified in the selection criteria in section I.A. of this document.
7. Once the eSTAR prepared 510(k) is received by FDA, FDA does not intend to conduct the RTA process. However, FDA intends to employ a technical screening process for the eSTAR like the one described in FDA draft guidance "Electronic Submission Template for Medical Device 510(k) Submissions" (Ref. 5). The technical screening process is a process for verifying that eSTAR responses accurately describe the device(s) (e.g., there are, in fact, no tissue contacting components if indicated as such) and that there is at least one relevant attachment per each applicable attachment-type question (e.g., a Software Description attachment is included in response to the Software Description question if software is applicable to the submission). The technical screening process is anticipated to occur within 15 calendar days of FDA receiving the 510(k) eSTAR. FDA intends to only begin the technical screening for 510(k) electronic submissions where the appropriate user fee has been paid. If the eSTAR is not complete when submitted, FDA

intends to notify the submitter via email and identify the missing information, and the 510(k) may be placed on hold until a complete replacement eSTAR is submitted to FDA. The remainder of the review will be conducted according to the FDA guidance "The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications" (Ref. 10), and the procedures identified in part 807, subpart E (21 CFR part 807, subpart E).

8. Following completion of the review of 510(k)s in the CBER voluntary eSTAR Pilot Program, participating manufacturers will have the opportunity to provide individual feedback on the CBER voluntary eSTAR Pilot Program through the procedures outlined on the "Voluntary eSTAR Program" web page (Ref. 7). Non-pilot participants are welcome to submit feedback to the Docket (see ADDRESSES).

During the CBER voluntary eSTAR Pilot Program, CBER staff intends to be available to answer questions from or concerns of pilot participants that may arise.

C. Targeted Questions for the CBER Voluntary eSTAR Pilot Program

FDA requests responses to the following questions about eSTAR from pilot program participants and stakeholders outside the pilot who want to submit comments to the docket.

(1) Is eSTAR able to integrate into your organization's business process?

(2) Are you able to open eSTAR, and are you able to add values to the structured data fields, as well as add attachments? Once entered and added, are the data retained after closing and reopening eSTAR?

(3) If you use Assistive Technology, are you able to navigate through and complete eSTAR?

(4) If eSTAR is not intuitive to use, why?

(5) Is the organization and content in eSTAR as expected?

(6) If applicable, did you experience any difficulties using the Electronic Submission Gateway to submit eSTAR?

(7) Is eSTAR able to accommodate PDF attachments that are of the size you typically would provide in a submission?

(8) If all the required questions (indicated by red or green indicators) are provided values, and all the required attachments are added, does eSTAR properly indicate it is complete on the first page, and are all the sections listed in the "Completed" column in the final section?

(9) Do you have any suggestions to improve the effectiveness of eSTAR in its purpose, or suggestions to improve the usability?

II. Paperwork Reduction Act of 1995

This notice refers to previously approved FDA collections of information. These collections of information are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3521). The collections of information in part 807, subpart E have been approved under OMB control number 0910-0120.

III. References

The following references are on display at the Dockets Management Staff (see ADDRESSES), and are available for viewing by interested persons between 9 a.m. and 4 p.m., Monday through Friday; they are also available electronically at https://www.regulations.gov. FDA has verified the website addresses, as of the date this document publishes in the *Federal Register*, but websites are subject to change over time.

1. MDUFA III Commitment Letter, available at: https://www.fda.gov/media/83244/download.

2. "eCopy Program for Medical Device Submissions: Guidance for Industry and Food and Drug Administration Staff," dated April 27, 2020; available at: https://www.fda.gov/media/83522/download.

3. MDUFA IV Commitment Letter, available at: https://www.fda.gov/media/102699/download.

4. "Refuse to Accept Policy for 510(k)s: Guidance for Industry and Food and Drug Administration Staff," dated September 13, 2019; available at: https://www.fda.gov/media/83888/download.

5. "Electronic Submission Template for Medical Device 510(k) Submissions: Draft Guidance for Industry and Food and Drug Administration Staff," dated September 29, 2021; available at: https://www.fda.gov/media/152429/download.

6. Premarket Notification 510(k) Process for CBER-Regulated Products at: https://www.fda.gov/vaccines-blood-biologics/development-approval-process-cber/premarket-notification-510k-process-cber-regulated-products.

7. Voluntary eSTAR Program, available at: https://www.fda.gov/medical-devices/how-study-and-market-your-device/voluntary-estar-program.

8. Electronic Submission Gateway, available at: https://www.fda.gov/industry/electronic-submissions-gateway.

9. Regulatory Submissions in Electronic and Paper Format for CBER-Regulated Products; available at: https://www.fda.gov/about-fda/center-biologics-evaluation-and-research-cber/regulatory-submissions-electronic-and-paper-format-cber-regulated-products.

10. "The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)]: Guidance for Industry and Food and Drug Administration Staff," dated July 28, 2014; available at: https://www.fda.gov/media/82395/download.

Dated: June 14, 2022.

Lauren K. Roth,

Associate Commissioner for Policy.

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